

REMARKS/ARGUMENTS

Status of the claims

Applicants have amended claims 1, 6, and 22. Support for the amendment of claim 1 may be found in the specification, for example, at page 17, lines 17-23 and page 9, lines 30-34. Claim 6 has been amended to remove recitation of the term "heterologous". Claims 17, 18, 20-46 have been withdrawn from further consideration as the result of a restriction requirement. However, claim 22 has been amended to depend from claim 1 in accordance with the restriction requirement. Applicants thank the Examiner for noting that Applicants had previously incorrectly identified the status of claim 19 as withdrawn. The status identifier of claim 19 has been corrected to read original. Support for new claim 48 may be found in the specification, for example, at page 28, lines 24-26. Support for new claim 49 may be found, for example in the specification, at page 9, lines 30-34. Support for new claim 50 may be found, for example in the specification, at page 10, line 30 - page 11, line 12. Thus, no new matter has been added. Claim 6 has been cancelled. Upon entry of this amendment, claims 1, 2, 6, 9-16, 19, 22, and 47-50 are pending for examination. Reconsideration is respectfully requested in light of the remarks which follow. Furthermore, Applicants respectfully urge the Examiner to rejoin appropriate withdrawn dependent claims upon the allowance of a generic base claim.

Claim rejections under 35 U.S.C. § 112, second paragraph - indefiniteness

Claims 6 and 9 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. To the extent that this rejection applies to the amended claims, Applicants respectfully traverse.

In making this rejection, the Examiner alleges that claims 6 and 9 are indefinite because the meaning of "heterologous" in claim 6 is unclear. *See* Office Action at page 3. Applicants have amended claim 6 to remove recitation of the term "heterologous", thus obviating this ground for rejection.

Claim rejections under 35 U.S.C. § 112, first paragraph - written description

Claims 1, 2, 6, 9-16, 19, and 47 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to satisfy the written description requirement. To the extent that this rejection applies to the amended claims, Applicants respectfully traverse.

The Examiner has maintained this rejection from the previous Office Action. In maintaining this rejection, the Examiner alleges that "[w]hile applicants' amendment requiring additional structure of the claimed genus is acknowledged, a sufficient structure to function relationship has not been established to meet the requirements of the written description guidelines, because applicants' amendment requiring that the claimed genus have "ligase activity" is not a sufficient functional limitation, as there exist many different types of ligase activity, such that the skilled artisan would not recognize that applicants were in possession of a majority of the members of the claimed genus by virtue of this broad functional description." See Office Action at page 4.

In the interest of expediting prosecution, Applicants have amended claim 1 to recite, in part, "wherein the TRAC1 polypeptide has ubiquitin ligase activity". Applicants respectfully submit that by virtue of this amendment, a sufficient functional limitation has been placed on the ligase activity of the present invention, as requested by the Examiner. The recitation of this further functional limitation would allow the skilled artisan to recognize that the Applicants are in possession of the claimed invention. In particular, adequate written description of "ubiquitin ligase activity" is provided in the specification at page 9, lines 32-34 (and the reference disclosed therein), which would allow the skilled artisan to be able to distinguish the ligase activity of the present invention from other ligases known in the art, such as, for example, DNA ligases.

Furthermore, Applicants respectfully bring to the Examiner's attention a decision by the Board of Patent Appeals and Interferences, *Ex parte Sun*, Appeal No. 2003-1993. In this case, the Board found that claims directed to sequences with 80% identity to a reference sequence were adequately described because the supporting specification provided a reference sequence and a functional assay for the activity of the encoded proteins. Applicants submit that

the facts in *Ex Parte Sun* closely mirror those in the present case, and thus, under the standard used by the Board in *Sun*, the claims of the present invention satisfy the written description requirement¹. In the present case, the sequence of a particular TRAC1 polypeptide is provided as a reference sequence (SEQ ID NO: 1), a per cent identity to that reference sequence is claimed, and functional assays for the genus of ubiquitin ligase enzymes are well known in the art, such as those disclosed in WO 01/75145, incorporated by reference in the present application. Thus, under the standard set forth in *Sun*, the claims of the present invention are supported by adequate written description in the specification.

In light of the foregoing, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for alleged lack of written description.

Claim rejections under 35 U.S.C. § 112, first paragraph - enablement

Claims 1, 2, 6, 9-16, 19, and 47 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. To the extent that this rejection applies to the amended claims, Applicants respectfully traverse.

The Examiner has also maintained this rejection from the previous Office Action. In maintaining this rejection, the Examiner alleges that "[w]hile applicants' amendment requiring additional structure of the claimed genus is acknowledged, a sufficient structure to function relationship has not been established to enable the scope of applicants' claimed invention, because applicants' amendment requiring that the claimed genus have "ligase activity" is not a sufficient functional limitation, as there exist many different types of ligase activity, such that the skilled artisan would require undue experimentation to practice the methods of the claimed genus by virtue of this broad functional description." *See* Office Action at page 4.

In the interest of expediting prosecution, Applicants have amended claim 1 to recite, in part, "wherein the TRAC1 polypeptide has ubiquitin ligase activity". Applicants respectfully submit that by virtue of this amendment, a sufficient functional limitation has been placed on the ligase activity of the present invention, as requested by the Examiner. In

¹ The claim at issue in *Sun* concerned a cell cycle protein, wee1, and recited in part, "a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1."

particular, enablement of "ubiquitin ligase activity" is provided in the specification at page 9, lines 32-34 (and the reference disclosed therein), which would allow the skilled artisan to practice the invention without undue experimentation and in a manner reasonably correlated with the scope of the claims (which now recite a specific type of ligase activity).

The practice of the claimed invention relies on the use of a TRAC1 polypeptide (SEQ ID NO: 1) and variants that have at least about 90% or greater identity to SEQ ID NO: 1, wherein the TRAC1 polypeptide has ubiquitin ligase activity. Thus, in order to practice the claimed method, the skilled artisan needs to have (1) access to a nucleic acid encoding TRAC1; (2) knowledge of how to alter the amino acid sequence of EDG-1 so that it is 90% - 99.9% identical to SEQ ID NO: 1; (3) methods for expressing and testing the activity of TRAC1 polypeptides that are 90% - 100% identical to SEQ ID NO: 1 either *in vitro* or *in vivo*; and (4) assays for determining the functional effect of test compounds on TRAC1 polypeptide activity. The specification and common knowledge in the art provides ample guidance that renders each of these steps easily performed by a skilled artisan in the fields of molecular biology and cell biology, such that no more than routine experimentation is required to practice the claimed invention.

Specifically, (1) the cDNA sequence of TRAC1 is provide in SEQ ID NO:1; (2) methods of isolating TRAC1 orthologs, variants, polymorphic variants, and conservatively modified variants that are at least about 90% identical to SEQ ID NO: 1 are well know in the art of molecular biology and are disclosed in the specification at page 24, line 5 - page 25, line 24; (3) methods for the expression of TRAC1 polypeptides are also well known in the arts of molecular and cell biology and biochemistry and are disclosed in the specification at page 25, line 30 - page 28, line 21; purification of TRAC1 polypeptides is disclosed in the specification at page 28, line 23 - page 31, line 14; assays for ubiquitin ligase activity of TRAC1 are disclosed in the specification at page 9, lines 32-34, and WO 01/75145, which is disclosed in the specification and incorporated by reference; and (4) assays for identifying modulators of TRAC1 polypeptides are disclosed in the specification at page 31, line 16 - page 40, line 10. These disclosures would

allow the skilled artisan to practice the presently claimed invention with no more than routine experimentation.

In light of the foregoing, Applicants respectfully submit that the claimed invention, as currently amended, is enabled and request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claim rejections under 35 U.S.C. § 102(a)

Claims 1, 2, 13, 15, 16, 19, and 47 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by U.S. Patent No. 5,180,662 ("Sitkovsky"). To the extent that this rejection applies to the amended claims, Applicants respectfully traverse.

To anticipate a claim, a reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found... in a single prior art reference." *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Examiner has also maintained this rejection from the previous Office Action. In maintaining this rejection, the Examiner states, "[i]t continues to be recognized that while Sitkovsky may or may not have been aware of the existence of applicants' disclosed "TRAC1 polypeptide", the methods taught by Sitkovsky anticipate the claimed methods. Sitkovsky specifically teaches a method for directly assaying cytotoxic T lymphocyte activation comprising: incubating cytotoxic T lymphocytes with one or more lymphocyte activating stimuli compounds and measuring the secretion of BLT-esterase resulting from activation of cytotoxic T lymphocytes." *See* Office Action at page 9.

Without conceding the Examiner's grounds for rejection, Applicants have amended claim 1 to recite, in part, "contacting the compound with a recombinant TRAC1 polypeptide". Sitkovsky discloses a cellular assay method comprising the steps of "incubating cytotoxic T lymphocytes with antigen-bearing target cells or with immobilized monoclonal antibody to the antigen receptor of T lymphocytes, and measuring the amount of BLT-esterase secreted by the T lymphocytes." *See* Sitkovsky at column 2, line 67 - column 3, line 4. In contrast to the presently claimed invention, Sitkovsky discloses the use of cytotoxic T

lymphocyte cell line clones, 2C, OE4, and BM10-37, which have not undergone recombinant manipulation to result in the expression of recombinant TRAC1.

As argued in the previous Office Action response, Sitkovsky is totally silent as to the expression of TRAC1 polypeptide in the cytotoxic T lymphocytes used in his experiments. Accordingly, assuming *arguendo*, that even if the cytotoxic T lymphocytes disclosed by Sitkovsky expressed a native TRAC1 polypeptide, this reference certainly does not teach or suggest a recombinant TRAC1 polypeptide, as recited in amended claim 1. Instead, because Sitkovsky provides absolutely no indication as to whether the TRAC1 protein is present, should be present, or even could be present in the non-modified cells used in this reference, Sitkovsky can provide no teaching or suggestion of a recombinant TRAC1 polypeptide, and thus, does not disclose this element of amended claim 1.

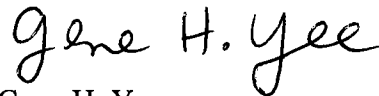
Because Sitkovsky does not teach or suggest each and every element of amended claim 1 as required to anticipate the claimed invention, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(a).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Gene H. Yee
Reg. No. 57,471

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
GHY:lls
61063914 v1